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# Comparison of mortality rates and functional results after transtibial and transfemoral amputations due to diabetes in elderly patients-a retrospective study

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## HIGHLIGHTS

- Mortality rates after trantibial and transfemoral amputations are high.
- Duration between surgery and death was significantly shorter in transfemoral amputees.
- Transtibial amputees have better mobility capacity than transfemorals.

## ARTICLE INFO

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## ABSTRACT

*Introduction:* This study aimed to compare mortality rates and functional results of transtibial and transfemoral amputations in elderly patients with diabetes.
*Methods:* 87 amputees [54 (62.1%) transtibial and 33 (37.9%) transfemoral] were included. Mean ages were 70.7 and 69.3 years in transfemoral and transtibial groups, respectively. Mean follow up time was 41.8 months. Amputee Mobility Predictor scores (with and without prosthesis) and Barthel Daily Living Index were used for functional evaluation of the survivors.
*Results:* First year mortality rates were 29.6% and 30.3% in transtibial and transfemoral groups, respectively. Overall mortality rate of both groups was 65.5% (66.7% in transtibial and 63.6% in transfemoral group). There was no difference between mortality rates of two groups. Duration between surgery and death was significantly shorter in transfemoral group. The mean Amputee Mobility Predictor scores (with prosthesis) of the transtibial and transfemoral groups were 32.3 and 26.9 points, respectively. The average Amputee Mobility Predictor scores (without prosthesis) of the transtibial and transfemoral groups were 29.5 and 22.7 points respectively. The differences between two groups' scores were significant. The mean Barthel Daily Living Index scores of the transtibial and transfemoral groups were 82.5 and 80.2 points respectively. The difference was not significant.
*Conclusions:* High mortality rates and morbidities after major lower limb amputations emphasize the importance of preventive measures and foot care in patients with diabetes.


## 1. Introduction

Lower extremity amputations are leading causes of morbidity and mortality in patients with diabetes [1–3]. In addition to macrovascular complications, e.g. myocardial infarction, stroke and peripheral vascular diseases, microvascular complications such as retinopathy and nephropathy may also be seen in these patients [1–6]. As a result of these complications, Diabetes Mellitus (DM) is accepted as the cause more than 50% of nontraumatic amputations and the risk of amputation is increased 12–15 folds in people with diabetes.(3–6) The incidence has been estimated as between 37 and 188 per 100.000 people [7,8].

Several factors may affect the functional outcomes of amputees. Increased age and amputation level would increase morbidity

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[7–12]. It was claimed that increased level of amputation may also increase mortality [3–6]. Although there are several studies related with these issues, there is a lack of literature reporting the updated mortality rates of these two major amputations and functional outcomes despite the advanced rehabilitation techniques and increase in quality of prosthesis technology. This study aims to discuss functional results of transtibial and transfemoral amputations due to incurable wounds in elderly patients with diabetes. We tried to compare mortality rates of these two major amputations and investigate the comorbidities of these patients.

## 2. Patients and methods

Between 1997 and 2013, total of 181 transtibial and transfemoral amputations (in 115 males and 60 females, 6 bilateral cases) were performed by five different surgeons in two third level orthopaedic centers. Patients who were younger than 60 years old of age, had a different level of amputation or amputated due to etiologies other than diabetes were excluded from the study. The wounds due to diabetes were determined to be the causes of amputations in 92 (50.8%) extremities of 87 patients. The demographic information, co-morbidities, complications were investigated from patients' charts retrospectively. The patients were called by phone and survivors were invited to the outpatient clinic for evaluation of the functional status. Amputee Mobility Predictor (AMP) scores were used to evaluate the survivor unilateral amputees [13]. The AMP scores of the patients were checked with prosthesis (AMPpro) and without prosthesis (AMPnopro). In addition, Barthel Daily Living Index was used for functional evaluation of all patients [14]. If the patient was dead, the time of death after surgery and the questions in Barthel Daily Living Index were asked to the relatives by phone regarding their final status. The outcomes were assessed by an author (AS). The study has local Institutional Review Board approval and informed consent was obtained from all patients.

The statistical analysis was performed by using SPSS 15 (SPSS INC., Chicago, IL; USA). The independent sample T test was used to compare the means of the hospital stay and functional results of the two groups. The Kaplan-Meier survival analysis was used with the death defined as end point. Comparison of survival curves was done by using Log Rank test. We checked for first and fifth years survivorships. The Cox regression analysis was used to detect factors related with mortality and to calculate the corresponding hazard ratios. The Fisher's Exact Test was used in order to compare distribution of comorbidities in two groups. A p value lesser than 0.05 was accepted as significant.

## 3. Results

Transtibial amputation was performed in 59 (64.1%) (five bilateral cases) and transfemoral in 33 (35.9%) extremities. In transfemoral group 23 patients were male and 10 were female. Mean age was 70.7 (range, 61–95) years at the time of amputation. Twenty of the patients had right and 13 had left extremity amputations. In transtibial group 33 patients were male and 21 were female. Mean age was 69.3 (range, 60–84) years at the time of amputation (Table 1). Thirty seven left sided and 22 right sided amputations were performed. Mean hospital stay was 10.1 (range, 2–62) days [9.8 (range, 2–33) days in transtibial group and 13.2 (range, 5–62) days in transfemoral group]. The difference between two groups was statistically significant. ($p = 0.024$).

The mortality rates were 29.6% and 30.3% in transtibial and transfemoral groups at the end of the first year, respectively. Five-year mortality rates were 66.7% in transtibial group and 63.6% in transfemoral group. Overall mortality rate was 65.5% for all amputees. There was no difference between mortality rates of two groups.($x^2 = 0.169$, $p = 0.681$ for first year and $x^2 = 0.156$, $p = 0.693$ for fifth year) (Figs. 1 and 2) The mean periods between amputation and death were 13.6 (range, 1–61) months in transtibial group and 7.1 (range, 1–40) months in transfemoral group. The difference was statistically significant.($p < 0.001$).

In three males and two females bilateral transtibial amputation was performed. Mean age of these five patients was 67.2 (range, 60–75) years, mean follow up was 34 (range, 17–40) months. Two of these patients died with a mean of 22 months after surgery.

Superficial infections occured in 10 (16.9%) extremities of the transtibial group and in 5 (15.2%) extremities of the transfemoral group during early postoperative follow ups. All patients were treated by antibiotics but debridement was needed in 7 (11.9%) extremities of transtibial group and 3 (9.1%) of the transfemoral group.

The comorbidities in transtibial group were chronic renal disease (CRD) in 3 patients, coronary artery disease (CAD) in 5 patients, chronic obstructive pulmonary disease (COPD) in 1 patient, chronic hepatic disease (CHD) in 1 patient. In transfemoral group 12 patients had CRD, 3 patients had CAD and 2 patients had COPD. The difference between two groups in terms of number of patients with CAD, COPD and CHD was not significant.($p = 0.979$, $p = 0.554$ and $p = 1$, respectively) In transfemoral group there were more patients with CRD.($p = 0.001$) In Cox regression analysis, CAD and COPD were found to be increasing mortality.($p < 0.001$) (Table 2).

The survivors of this cohort [30 patients- 18 transtibial, 12 transfemoral] were evaluated for functional status. Mean age of those patients was 72.3 (range, 65–89) years. There were 10 males and 8 females in transtibial group [mean age, 74.1 (range, 65–87) years]. Transfemoral group included 6 males and 6 females [mean age, 71.2 (range, 67–89) years]. The overall mean follow up time was 79.1 (range, 25–129) months. Average follow up times were 88.9 (range, 31–129) months in transtibial group and 69.5 (range, 25–104) months in transfemoral group. The mean AMPpro scores of the transtibial and transfemoral groups were 32.3 (range, 14–42) and 26.9 (range, 19–40) points, respectively. The average AMPnopro scores of the transtibial and transfemoral groups were 29.5 (range, 11–40) and 22.7 (range, 16–39) points, respectively. The differences between two groups' scores were statistically significant (Table 3).

The Barthel scores were determined by interview with relatives of the dead patients and the outpatient clinic evaluation of the survivors. The mean scores of the transtibial and transfemoral groups were 82.5 (range, 70–100) and 80.2 (range, 65–100) points, respectively. The difference between two groups was not statistically significant.($P = 0.21$) (Table 3).

## 4. Discussion

Peripheral vascular disease and diabetes mellitus are major causes of lower-limb amputations [3]. More than half of the non-traumatic amputations are related to the complications of diabetes. Additionally it has been shown that diabetes increases the risk of amputation for 12–17 times [4,5]. In our study as consistent with the literature, foot wounds due to diabetes (50.8%) were leading cause of major amputations.

In the literature the mortality rates were between 20.8 and 30.2% for transtibial amputations and 35.4–46.2% for transfemoral amputations at the end of first year [3,6,9–11]. In their study in which 2375 patients were included; Bates et al. had found that mortality rates were higher in the transfemoral amputation group than the transtibial group [3]. Carmona et al. reported survival rates after major lower limb amputation at the first year as 61.7%, at the second year as 47.9%, at the fifth year as 22.6% and at the tenth year as 13%. They claimed that 10.5% of patients died at the first days of hospitalization and transtibial amputation group had less mortality

**Table 1**
Demographic data of the patients.

| Parameter | Value |
|---|---|
| **Number of transtibial amputees** | **54 (59 extremity)** |
| Male | 33 |
| Female | 21 |
| Mean age (years) | 69.3 (range, 60–84) |
| **Number of transfemoral amputees** | **33** |
| Male | 23 |
| Female | 10 |
| Mean age (years) | 70.7 (range,61–95) |
| **Mean hospital stay (days)** | **10.1 (range, 2–62)** |
| Transtibial group | 9.8 (range, 2–33) |
| Transfemoral group | 13.2 (range, 5–62) |
| **Comorbidities in Transtibial group (number of patients)** | **10** |
| Chronic Renal Disease | 3 |
| Coronary Artery Disease | 5 |
| Chronic Obstructive Pulmonary Disease | 1 |
| Chronic Hepatic Disease | 1 |
| **Comorbidities in Transfemoral group (number of patients)** | **17** |
| Chronic Renal Disease | 12 |
| Coronary Artery Disease | 3 |
| Chronic Obstructive Pulmonary Disease | 2 |
| **Mean follow up of survivors (months)** | **79.1 (range, 25–129)** |
| Transtibial group | 88.9 (range, 31–129) |
| Transfemoral group | 69.5 (range, 25–104) |

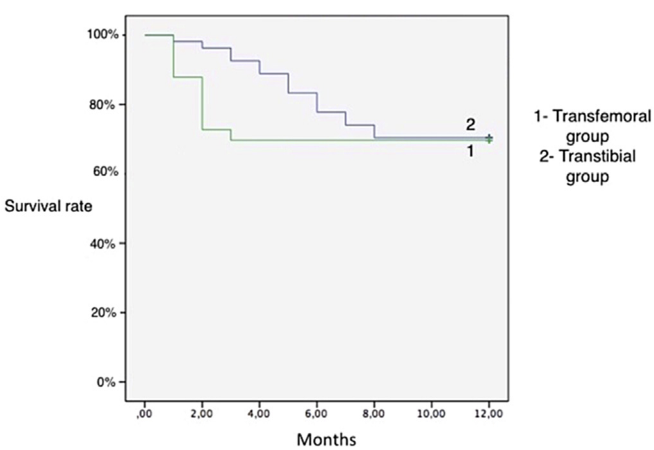


**Fig. 1.** The Kaplan-Meier survival analysis of first year. The end point was defined as death. The time between surgery and death was shorter in transfemoral group but at the end of the first year there was no significant difference between two groups. "+" indicates cencored data.

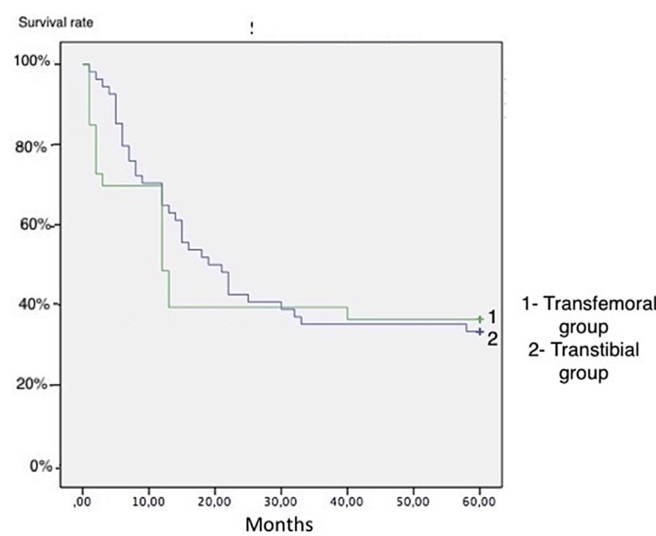


**Fig. 2.** The Kaplan-Meier survival analysis of fifth year. The end point was defined as death. "+" indicates cencored data.

rate than the higher level amputations. Authors correlate this difference with co-morbidities [6]. The first and fifth years mortality rates of our patients were 29.6% and 66.7% in transtibial group and 30.3% and 63.6% in transfemoral group, respectively. The overall mortality rate was 65.5%. Our results were consistent with literature. Although there was no difference between mortality rates of two groups, it can be seen that duration between surgery and death was shorter in transfemoral amputees (Fig. 1). We have no data which could explain this finding since distributions of two mortality increasing factors were similar in two groups. Our opinion is that delay in both, hospital admission and appropriate treatment would end up with higher amputation level and shorter survival time.

The higher mortality rates after major lower limb amputations can be explained with the comorbidities. In several studies the mortality related situations after major lower limb amputations has been investigated and it was claimed that congestive heart disease, atrial fibrillation, chronic obstructive lung disease, dementia, cerebrovascular disease, hemodialysis and obesity increased the mortality [6,15,16]. Aulivola et al. calculated overall 30-day mortality for such patients as 8.6% and they emphasized that cardiac complications, sepsis and pneumonia are the leading causes of death [11]. In our study, we found that CAD and COPD were increasing mortality.($p < 0.001$).

**Table 2**
Cox regression analysis with death as end point. *The comorbidities which effect mortality. Values are expressed as mean, with 95% confidence interval in parentheses.

| Comorbidity | Hazard ratio | p Value |
|---|---|---|
| Chronic Renal Disease | 0.701 (0.33–1.489) | 0.355 |
| Coronary Artery Disease* | 0.155* (0.060–0.399) | <0.001* |
| Chronic Obstructive Pulmonary Disease* | 0.084* (0.023–0.306) | <0.001* |
| Chronic Hepatic Disease | 0.211 (0.028–1.594) | 0.132 |

**Table 3**
Mean Amputee Mobility Predictor (AMP with and without prosthesis) and Barthel scores.

| Scores | Transtibial group (n:54 patients) | Transfemoral group (n:33 patients) | p Value |
|---|---|---|---|
| AMPpro | 32.3 (14–42) | 26.9 (19–40) | 0.024 |
| AMPnopro | 29.5 (12–34) | 22.7 (11–32) | 0.021 |
| Barthel | 82,5 (70–100) | 80,2 (65–100) | 0.34 |

Bilateral amputation was performed in five patients. One of them had simultaneous bilateral transtibial amputation. The others were operated at different times. Peters et al. emphasized that the incidence of bilateral amputation was higher in people with diabetes [17]. Mac Neill et al. found mortality rate as 39% and life expectancy as 4.2 years after surgery, in their study which consists 82 bilateral transtibial amputees. The cause of the amputations were diabetes and peripheral artery disease. Recent studies suggest that life expectancy in bilateral amputation group was higher than unilateral group [18,19]. They concluded that most of the unilateral amputees do not survive long enough to undergo bilateral amputation. In our study mean follow up for these patients was 34 months and over all mortality rate was 40%.

Norvell et al. reported 41% and 29% mobility success rate according to Locomotor Capability Index in patients with transtibial and transfemoral amputations, respectively. Authors claimed that patients who achieved mobility success had a higher satisfaction rates [20]. In their study which investigates functional status of amputee with diabetes, Attinger and Brown reported 64% ambulation rate in transtibial amputees [21]. Larsson et al. emphasized that 61% of patients with major lower extremity amputation returned to living independently [22]. Machado Vaz et al. analysed functional and psychological results of lower limb amputees. The data showed that the amputees had high risk of depression and their functional capacities were significantly decreased [23]. We calculated AMP score with and without prosthesis. In our study the mean AMPpro scores of the transtibial and transfemoral groups were 32.3 and 26.9 points respectively. The average AMPnopro score of the transtibial group was 29.5 points and transfemoral group was 22.7 points. The differences between two groups were statistically significant (Table 3). This can be interpreted as transtibial group has better mobility capacity than transfemoral group. Waters et al. reported better functional results and less energy expenditure with lower level of amputations [24]. Nehler et al. compared transtibial and transfemoral amputees in their study which consists of 172 major amputations. Although transtibial group had better results by means of ambulation, there was no statistically significant difference between two groups [25].

Pernot et al. investigated 164 patients with major lower limb amputations. The study consists of amputations due to diabetes but also tumors, vascular diseases and trauma [26]. The authors reported mean Barthel Index score as 79 points. In our study mean Barthel scores of the transtibial and transfemoral groups were 82.5 and 80.2 points respectively. The difference between two groups was not significant.($p = 0.34$).

In our series mean length of hospital stay was calculated as 10.1 days. The transfemoral group had significantly longer hospitalization than transtibial group in our study. The reason for longer hospitalization might be associated with long surgical preparation time and postoperative care. Longer surgical preparation time can be due to those patients' irregular blood glucose profile and comorbidities. Besides, post-surgical complications may be encountered with the same reasons. High complication risk may increase the length of hospital stay. As it is expected, causes of higher amputation level might indicate longer hospitalization.

The cause of amputations in our study was incurable wounds. Ulcer care (debridement + antibiotics), hyperbaric oxygen therapy and soft tissue reconstructions can be listed as parts of classic ulcer treatment [27]. Several growth factors; e.g. transforming growth factor β2, recombinant human platelet-derived growth factor, recombinant human epidermal growth factor, recombinant human basic fibroblast growth factor; were reported as effective in diabetic wound care, recently [28]. But we believe that preventive measures (foot care programmes, special footwear and foot screenings) are most important factors that could decrease morbidity and mortality.

The level of amputation is decided according to the revascularization status of the extremity, severity of the wounds and infection. Some surgeons prefer aggresive revascularization in order to prevent high level amputations but some surgeons prefer higher level of amputations instead of aggresive revascularization [29]. The vascular surgery team plays critical role in decision making. It was shown that, increased level of amputation is associated with higher energy expenditure during ambulation with prosthesis [30]. This condition may cause increase in cardiovascular complication risk [31]. Devan et al. demonstrated that spinal and pelvic movement asymmetries during gait were more obvious following transfemoral amputation compared with transtibial amputation [32]. In addition risk of osteoarthritis increases with higher amputation levels [33]. In our opinion, these factors are related with difference in functional outcomes of two amputation groups. We don't have any data about gait or energy expenditure of these two groups but according to literature and our results, despite similar mortality rates we could advise to spend more efforts for soft tissue management and revascularization procedures in order to prevent higher level amputations for patients with diabetic foot ulcers.

The main limitations of this study are its retrospective design and small sample size. The numbers of patients with different comorbidities were not equal. Therefore effect of comorbidities on mortality can not be investigated reliably. Prospective multicenter studies with larger patient population and close number of patients in subgroups with comorbidities are necessary to investigate the answer of this question. In addition we collected the data about last functional status of the dead amputees via telephone interview with their relatives. This point decreases the reliability of the data. We evaluated functional outcomes only by using questionnaires. Gait analysis and measurements of energy expenditure during gait or other activites may be added to compare these two amputation types better. We don't have joint specific physical or radiologic examination findings. Therefore we could not make comments about the causes of difference between two groups. Those are important limitations of almost all of the studies about this issue. Addition of these data would increase the reliability of the studies.

## 5. Conclusion

High mortality rates after major lower extremity amputations point the importance of protective measures and foot care. The decrease in life span with increased amputation level and morbidities made us think to protect the extremity as long as possible.

Our results show that despite increased health care qualities, complications of diabetes still threaten lifes.

## Ethical approval

The ethical approval was given by local Institutional Review Board. Reference number: 10840098-185.

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## Author contribution

- Ali Seker, study design, data collections, data analysis, writing.
- Adnan Kara, writing.
- Savas Camur, data collections, data analysis.
- Melih Malkoc, writing.
- Mehmet Mesut Sonmez, data collections, data analysis.
- Mahir Mahirogullari, writing.

## Conflict of interest

None.

## Guarantor

Ali Seker.

## References

[1] P. Clarke, A. Gray, R. Legood, A. Briggs, R. Holman, The impact of diabetes-related complications on healthcare costs: results from the United Kingdom Prospective Diabetes Study (UKPDS Study No. 65), Diabet. Med. 20 (2003) 442–450.
[2] B.C. Callaghan, E. Feldman, J. Liu, K. Kerber, R. Pop-Busui, H. Moffet, et al., Triglycerides and amputation risk in patients with diabetes: ten-year follow-up in the DISTANCE study, Diabetes Care 34 (2011) 635–640.
[3] B. Bates, M.G. Stineman, D.M. Reker, J.E. Kurichi, P.L. Kwong, Risk factors associated with mortality in veteran population following transtibial or transfemoral amputation, J. Rehabil. Res. Dev. 43 (2006) 917–928.
[4] A.D. Morris, R. McAlpine, D. Steinke, D.I. Boyle, A.R. Ebrahim, N. Vasudev, et al., Diabetes and lowerlimb amputations in the community. A retrospective cohort study. DARTS/MEMO collaboration. Diabetes audit and research in tayside scotland/medicines monitoring unit, Diabetes Care 21 (1998) 738–743.
[5] J.V. Selby, D. Zhang, Risk factors for lower extremity amputation in persons with diabetes, Diabetes Care 18 (1995) 509–516.
[6] G.A. Carmona, P. Hoffmeyer, F.R. Herrmann, J. Vaucher, O. Tschopp, A. Lacraz, et al., Major lower limb amputations in the elderly observed over ten years: the role of diabetes and peripheral arterial disease, Diabetes Metab. 31 (2005) 449–454.
[7] S.K. Shah, J.F. Bena, M.T. Allemang, R. Kelso, D.G. Clair, L. Vargas, V.S. Kashyap, Lower extremity amputations: factors associated with mortality or contralateral amputation, Vasc. Endovasc. Surg. 47 (8) (2013 Nov) 608–613.
[8] T.R. Dillingham, L.E. Pezzin, E.J. MacKenzie, Limb amputation and limb deficiency: epidemiology and recent trends in the United States, South Med. J. 95 (8) (2002) 875–883.
[9] J. Feinglass, W.H. Pearce, G.J. Martin, J. Gibbs, D. Cowper, M. Sorensen, et al., Postoperative and late survival outcomes after major amputation: findings from the department of veterans affairs national surgical quality improvement program, Surgery 130 (2001) 21–29.
[10] T. Pohjolainen, H. Alaranta, J. Wikstrom, Primary survival and prosthetic fitting of lower limb amputees, Prosthet. Orthot. Int. 13 (1989) 63–69.
[11] B. Aulivola, C.N. Hile, A.D. Hamdan, M.G. Sheahan, J.R. Veraldi, J.J. Skillman, et al., Major lower extremity amputation: outcome of a modern series, Arch. Surg. 139 (2004) 395–399.
[12] T. Schoppen, A. Boonstra, J.W. Groothoff, J. de Vries, L.N. Göeken, W.H. Eisma, Physical, mental, and social predictors of functional outcome in unilateral lower-limb amputees, Arch. Phys. Med. Rehabil. 84 (6) (2003 Jun) 803–811.
[13] R.S. Gailey, K.E. Roach, E.B. Applegate, B. Cho, B. Cunniffe, S. Licht, et al., The amputee mobility predictor: an instrument to assess determinants of the lower-limb amputee's ability to ambulate, Arch. Phys. Med. Rehabil. 83 (2002 May) 613–627.
[14] C. Collin, D.T. Wade, S. Davies, V. Horne, The Barthel ADL Index: a reliability study, Int. Disabil. Stud. 10 (1988) 61–63.
[15] T.C. Collins, M. Johnson, J. Daley, W.G. Henderson, S.F. Khuri, H.S. Gordon, Preoperative risk factors for 30-day mortality after elective surgery for vascular disease in Department of Veterans Affairs hospitals: is race important? J. Vasc. Surg. 34 (2001) 634–640.
[16] I. Kantonen, M. Lepantalo, M. Luther, J.-P. Salenius, K. Ylonen, Factors affecting the results of surgery for chronic critical leg ischemia- a nationwide survey, J. Vasc. Surg. 27 (1998) 940–947.
[17] E.J. Peters, M.R. Childs, R.P. Wunderlich, L.B. Harkless, D.G. Armstrong, L.A. Lavery, Functional status of persons with diabetes-related lower-extremity amputations, Diabetes Care 24 (2001) 1799–1804.
[18] H.L. Mac Neill, M. Devlin, T. Pauley, A. Yudin, Long-term outcomes and survival of patients with bilateral transtibial amputations after rehabilitation, Am. J. Phys. Med. Rehabil. 87 (2008) 189–196.
[19] J. Kulkarni, S. Pande, J. Morris, Survival rates in dysvascular lower limb amputees, Int. J. Surg. 4 (2006) 217–221.
[20] D.C. Norvell, A.P. Turner, R.M. Williams, K.N. Hakimi, J.M. Czerniecki, Defining successful mobility after lower extremity amputation for complications of peripheral vascular disease and diabetes, J. Vasc. Surg. 54 (2011) 412–419.
[21] C.E. Attinger, B.J. Brown, Amputation and ambulation in diabetic patients: function is the goal, Diabetes Metab. Res. Rev. 28 (1) (2012) 93–96.
[22] J. Larsson, C.D. Agardh, J. Apelqvist, A. Stenström, Long-term prognosis after healed amputation in patients with diabetes, Clin. Orthop. Relat. Res. 350 (1998) 149–158.
[23] I. Machado Vaz, V. Roque, S. Pimentel, A. Rocha, H. Duro, Psychosocial characterization of a Portuguese lower limb amputee population, Acta Med. Port. 25 (2012) 77–82.
[24] R.L. Waters, J. Perry, D. Antonelli, H. Hislop, Energy cost of walking of amputees: the influence of level of amputation, J. Bone Jt. Surg. Am. 58 (1976) 42–46.
[25] M.R. Nehler, J.R. Coll, W.R. Hiatt, J.G. Regensteiner, G.T. Schnickel, W.A. Klenke, et al., Functional outcome in a contemporary series of major lower extremity amputations, J. Vasc. Surg. 38 (2003) 7–14.
[26] H.F. Pernot, G.M. Winnubst, J.J. Cluitmans, L.P. De Witte, Amputees in Limburg: incidence, morbidity and mortality, prosthetic supply, care utilisation and functional level after one year, Prosthet. Orthot. Int. 24 (2000) 90–96.
[27] S. O'Meara, N. Cullum, M. Majid, T. Sheldon, Systematic reviews of wound care management: (3) antimicrobial agents for chronic wounds; (4) diabetic foot ulceration, Health Technol. Assess. 4 (2000) 1–237.
[28] A.J. Martí-Carvajal, C. Gluud, S. Nicola, D. Simancas-Racines, L. Reveiz, P. Oliva, et al., Growth factors for treating diabetic foot ulcers, Cochrane Database Syst. Rev. 10 (2015 Oct 28) CD008548, http://dx.doi.org/10.1002/14651858.
[29] K. Matsuzaki, R. Hayashi, K. Okabe, N. Aramaki-Hattori, K. Kishi, Prognosis of critical limb ischemia: major vs. minor amputation comparison, Wound Repair Regen. 23 (5) (2015 Sep) 759–764.
[30] B.D. Suckow, P.P. Goodney, R.A. Cambria, D.J. Bertges, J. Eldrup-Jorgensen, J.E. Indes, et al., Vascular Study Group of New England. Predicting functional status following amputation after lower extremity bypass, Ann. Vasc. Surg. 26 (1) (2012 Jan) 67–78.
[31] J.E. Naschitz, R. Lenger, Why traumatic leg amputees are at increased risk for cardiovascular diseases, QJM 101 (4) (2008 Apr) 251–259.
[32] H. Devan, A. Carman, P. Hendrick, L. Hale, D.C. Ribeiro, Spinal, pelvic, and hip movement asymmetries in people with lower-limb amputation: systematic review, J. Rehabil. Res. Dev. 52 (1) (2015) 1–19.
[33] J. Kulkarni, J. Adams, E. Thomas, A. Silman, Association between amputation, arthritis and osteopenia in British male war veterans with major lower limb amputations, Clin. Rehabil. 12 (4) (1998 Aug) 348–353.